DISSERTATION ON

THE CLINICAL AND ELECTROPHYSIOLOGICAL EVALUATION OF NEUROPATHY IN RHEUMATOID ARTHRITIS

Submitted in partial fulfilment of

Requirements for

BRANCH I – D.M., NEUROLOGY

of

THE TAMILNADU DR.M.G.R MEDICAL UNIVERSITY

CHENNAI

MADRAS MEDICAL COLLEGE

CHENNAI – 600 003.

AUGUST 2007

CERTIFICATE

This is to certify that this dissertation entitled "**THE CLINICAL AND ELECTROPHYSIOLOGICAL EVALUATION OF NEUROPATHY IN RHEUMATOID ARTHRITIS**" submitted by **Dr. S. SUNDAR appearing** for **D.M.,** Degree examination in **August 2007**, is a bonafide record of work done by him under my direct guidance and supervision, in partial fulfillment of regulations of the Tamil Nadu Dr. M.G.R. Medical University, Chennai. I forward this to the Tamil Nadu Dr. M.G.R. Medical University, Chennai, Tamil Nadu, and India.

HEAD OF THE DEPARTMENT,
Institute of Neurology,
Government General Hospital
Chennai – 600 003

PROFESSOR OF NEUROLOGY,
Institute of Neurology,
Madras Medical College
Government General Hospital
Chennai – 600 003

DEAN
Madras Medical College
Government General Hospital
Chennai – 600 003

DECLARATION

I solemnly declare that the dissertation titled "**THE CLINICAL AND ELECTROPHYSIOLOGICAL EVALUATION OF NEUROPATHY IN RHEUMATOID ARTHRITIS "** is done by me at the Institute Of Neurology, Madras Medical College & Govt. General Hospital, Chennai during 2005-2007 under the guidance and supervision of Prof**. V. Natarajan.**

The dissertation is submitted to The Tamilnadu Dr. M.G.R. Medical University towards the partial fulfillment of requirements for the award of D.M., in Neurology.

Place: Chennai

Date: 26/05/2007

Dr. S. Sundar
Postgraduate Student
D.M. in Neurology,
Madras Medical College
Chennai

SPECIAL ACKNOWLEDGMENT

I gratefully acknowledge and sincerely thank

Prof. Dr T. P. KALANIDHI ,The DEAN, Madras Medical College and Government General Hospital, Chennai for allowing me to do this Dissertation and utilize the institutional facilities.

ACKNOWLEDGEMENT

I would like to express my sincere gratitude to my beloved Professor and Head, Institute of Neurology, **Prof. Geetha Lakshmipathy,** without whose inspiration, expert opinion, guidance, this study would not have been possible.

I profoundly thank my beloved Professors, **Prof. K. Muthuraj, Prof. A. V. Srinivasan and Prof. R. M. Boopathy** for their valuable guidance, encouragement and valuable criticism.

This is one another fine moment to express my gratitude and indebtedness to my beloved Chief, **Prof. V. Natarajan,** for his motivation, kind words of advice, which enabled me to complete this work.

I am extremely thankful to Assistant Professors of Neurology **Dr. V. Kamaraj, Dr. Mutharasu, Dr. K. Bhanu, Dr. S. Balasubramaniam and Dr. S. Velusamy** for their co-operation and guidance.

I also thank the Chief **Prof. C. Panchapakesa Rajendran,**
Assistant Professors and Post graduates of the Department of Rheumatology for their valuable help throughout the study.

I am thankful to all my Postgraduate colleagues for their constant support

and sharp constructive criticism.

I am thankful to the technicians and staffs of Neurochemistry laboratory, Radiology Department and our EMG laboratory for their cooperation.

Last but not the least, I thank each patient for the whole-hearted cooperation despite the morbidity they suffered.

CONTENTS

INTRODUCTION

Rheumatoid arthritis is a chronic inflammatory polyarthritis leading to deformities. It is defined by the American College of Rheumatology (ACR) as a diffuse connective disease, and around 40% of patients are considered to have characteristic extra-articular manifestations. The predominant extra-articular manifestations involve the lungs, nerves, blood vessels, heart, skin, eyes[1].

Neuropathy is one of the important extra-articular manifestations of Rheumatoid arthritis and can have crippling consequences[44,72]. Subjective and objective assessment of neuropathy in RA is difficult due to concomitant joint disease as both may contribute to muscle wasting and weakness. Neuropathy in RA is most commonly due to vasculitis, entrapment or due to drugs. Various types of neuropathy can occur from mononeuritis multiplex to severe sensorimotor neuropathy. Although there might be some recovery of the predominant sensory neuropathy, severe mixed neuropathy or mononeuritis multiplex appears to be a reflection of an aggressive vasculitic form of RA and is associated with poor prognosis. Hence it is imperative that rheumatoid neuropathy is detected at the earliest when it is sub clinical. Electrophysiological studies are important for confirmation of clinical suspicion and to detect sub clinical neuropathy.

Paucity of Indian literature on rheumatoid neuropathy creates a lacuna in the critical evaluation and discussion of the subject. Hence this study was carried out to find out the incidence and pattern of neuropathy in our RA patients. Another aim was to find out any correlation between neuropathy and disease parameters like duration, activity, rheumatoid factor.

AIMS OF THE STUDY.

- To find out the incidence and pattern of neuropathy in Rheumatoid arthritis.

- To correlate neuropathy with disease parameters of Rheumatoid arthritis and other extra-articular manifestations.

REVIEW OF LITERATURE

HISTORY

Sporadic references to peripheral neuropathy complicating RA appeared as early as the last century. Pitres & Vaillard (1886) and later Bannatype (1898) reported involvement of peripheral nerves in RA. In 1942, Ball called attention to the clinical significance of systemic involvement that included peripheral nerves. In 1952, Hart, Golding & Mckenzie[39] were the first to describe a definite series of ten patients with peripheral neuropathy complicating RA and was thought to be caused by diffuse arteritis. In 1965, Bennet & Scott described rheumatoid neuropathy associated with autonomic neuropathy. In 1965, C.A.Pallis & J.J.Scott[14] described 30 cases of RA with peripheral neuropathy. They described 5 patterns of neural involvement namely

1. Upper limb with lesions in major peripheral nerve.
2. Upper limb with digital neuropathy.
3. Lower limb with lesions in major peripheral nerve.
4. Lower limb with distal sensory neuropathy.
5. Distal sensorimotor Polyneuropathy of upper limb & lower limb.

Marmor et al in 1967, Chamberlain & Carbett[42] in 1970, Lloyd & Agarwal[2] in 1970 defined rheumatoid neuropathy as a separate entity & it should not be confused with compressive neuropathy.

RHEUMATOID ARTHRITIS: A SHORT GENERAL DESCRIPTION

EPIDEMIOLOGY :

RA is a chronic inflammatory disorder affecting primarily the synovial-lined joints. RA is widely distributed all over the world and affects all races[6]. The prevalence in the adult population is assessed at approximately 0.8 to 1.0%. The incidence varies in different geographical areas from 27 to 8 / 100000[9]. Prevalence and incidence are about 3 times higher in women than in men and increases with age.

ETIOLOGY :

Both genetic predisposition and environmental factors are likely to play a role[10]. RA is associated with HLA-DR4. Patients with DR-4 positive show more disease activity and continued progression of arthrogenic changes[12]. Possible environmental factors are infectious agents, but evidence for a role of any specific microorganism has not been discovered yet.[16]

PATHOGENESIS:

Very schematically, the following might happen: an as yet unidentified, arthritogenic stimulus triggers an immuno-inflammatory cascade in an immuno-genetic susceptible individual. Inflammation is mediated by inflammatory cells, prostaglandins, and cytokines. The inflammation causes local joint damage and widespread bone loss.[21,25]

Rheumatoid factor (RF), one of the altered immunoglobins in RA, is an auto-antibody against IgG. It is present in approximately 80% of RA patients, and is not specific for RA despite its name. RF's are involved in immune-complex formation and induce recruitment of macrophages and other white blood cells[28]. RA patients with a positive test for RF in blood have a severe clinical disease[30]. Extra-articular manifestations occur mostly in RF positive

patients with progressive joint inflammation, suggesting these manifestations are immune-mediated.

PATHOLOGY :

PANNUS: The synovia become thickened, in part due to inflammatory infiltrate and to oedema, but also because of growth of blood vessels, proliferation of synovial fibroblasts, and multiplication and enlargement of synovial lining cells. This granulation tissue is called pannus. The pannus attacks the cartilage causing destruction and also invade the bone cortex near the joints.

NODULES: Nodules are found in 20-30% of patients with definite seropositive RA. The nodule has a yellow, necrotic centre that has at microscopy a fibrinoid aspect. It is mainly located subcutaneously at pressure points: at the extensor side of the olecranon, the proximal part of the ulna.[31,32]

VASCULITIS: vasculitis in RA may affect arteries of all sizes as well as small vessels, but has a preference for medium and small arteries[35]. Though all layers may be infiltrated, inflammation is generally greatest in the adventitia. It is considered to be mediated by the deposition of circulating immune complexes[37].

CLINICAL FEATURES AND DIAGNOSIS :

RA presents with systemic manifestations or with symptoms and signs of arthritis of metacarpophalangeal joints, proximal interphalangeal joints or wrists[25]. More proximal, larger joints may become involved with time. Onset is gradual or occasionally acute. Joint inflammation causes morning stiffness, limitation of movement, pain, swelling, redness, and

deformity. Not all of these changes are always detectable at examination. Active vasculitis is seen in all patients with joint deformities and high RF titre, and is, in some cases (not always), acute and dramatic in onset. It may cause a large number of clinical manifestations, including nail fold teleangiectasia, digital gangrene, purpura, skin ulcers, visceral infarcts, and mononeuritis multiplex. CNS involvement is rare but has been reported.

Laboratory examination in patients with RA shows increase of erythrocyte sedimentation rate (ESR) and some degree of anemia and leukocytosis. A raised RF is in favour of the diagnosis. X-rays reveal periarticular osteopenia and marginal erosions.

Diagnosis is made mainly on clinical grounds. As a rule, joints are affected in a symmetrical fashion or with some degree of asymmetry. The main exceptions to this rule are the joints in the paretic side of hemiplegic individuals, which are much less involved probably due to limitation of activity.

The 1988 revised ACR classification criteria[71] for definite RA are given below.

NO	CRITERION	DEFINITION
1.	MORNING STIFFNESS	Morning stiffness in and around the joints lasting at least 1 hour before maximal improvement.
2	ARTHRITIS OF 3 MAJOR JOINTS	At least 3 joint areas having soft tissue swelling or fluid observed by a physician among PIP,MCP,WRIST,KNEE,ANKLE,AND MTP JOINTS
3	ARTHRITIS OF HAND JOINTS	At least one joint area swollen as above in wrist, MCP,PIP
4	SYMMETRICAL ARTHRITIS	Simultaneous involvement of same joint areas on both sides

5	RHEUMATOID NODULES	Subcutaneous nodules over bony prominences observed by physician
6	RHEUMATOID FACTOR	Demonstration of abnormal amounts of serum RF by a method that has been positive in less than 5 % of normal subjects
7	RADIOGRAPHIC CHANGES	Erosions or unequivocal bony calcification

EXTRA-ARTICULAR MANIFESTATIONS OF RA are as follows.

I. Essential to systemic rheumatoid disease

Nodules

Pericarditis, pleuritis

Vasculitis including neuropathy .

II. Other features and associated syndromes

Anemia

Lymphadenopathy

Osteopenia

Sjogren's syndrome

Interstitial lung fibrosis

Amyloidosis

Felty's syndrome.

THERAPY

Therapy aims at relief of pain and stiffness and preservation or improvement of function. Scales have been developed to assess the functional status of patients and to measure disease activity[39]. Non-pharmaceutical interventions (psychosocial assistance, physical therapy, occupational therapy, splints and orthoses, surgery) have an important place in treatment plans. Pharmaceutical interventions are either local (intra-articular injections, ulcer treatment) or systemic. Among the latter, one makes a distinction between non-steroidal inflammatory drugs (NSAIDs), corticosteroids, and a heterogeneous group of disease-modifying antirheumatic drugs (DMARDs), which are also called slow-acting antirheumatic drugs (SAARDs). Drugs belonging to this last group are hydroxychloroquine, gold salts, sulfasalazine, D-penicillamine, azathioprine, methotrexate, cyclosporine, and cyclophosphamide. Early intensive therapy with prednisolone and methotrexate is at present advocated.

COURSE OF THE DISEASE AND PROGNOSIS

In some patients, the course is intermittent (15-20%); occasionally, it has long clinical remissions (10%); but in most patients, it is progressive (60-70%). Life expectancy is shortened, more for males than for females. Seropositivity and onset at a young age are associated with a poorer prognosis.

NEUROLOGY OF RHEUMATOID ARTHRITIS

1. MOOD AND COGNITION:

Patients with RA are more often depressed and anxious than age and sex matched controls[40]. Feelings of distress are increased by pain, disability, and fatigue. Mild cognitive deficits were found in a recent well-controlled, extensive neuropsychological investigation of a group of nonneurological patients

with RA[41]. The result came as a surprise and could not be explained as an effect of psychological distress.

2. MENINGEAL NODULES, PACHYMENINGITIS, AND CNS VASCULITIS.

Rheumatic nodules occur occasionally in the dura, falx cerebri, the leptomeninges, and the choroid plexus[43]. Some of the nodules adhere to the brain or spinal cord and compress structures, but they do not intrude into the parenchyma and probably do not occur in the parenchyma of the nervous tissue. In some cases, not only nodules are present; there is also a more widespread, plaque-like inflammation of the meninges with necrosis, lymphocytes, and a variable percentage of plasma cells. This aseptic pachymeningitis may also occur on its own without any rheumatic nodules.[44] Vasculitis, extending in some cases from a region of pachymeningitis into the brain, has also been reported.

Mental obtundation, Organic brain syndrome, severe headache , seizures , cranial neuropathy including optic neuropathy , paresis and agnosia, thoracic myelopathy, and radiculopathy due to rheumatic nodules or pachymeningitis have all been reported. The number of patients with these syndromes is small and few reports are of recent date. Inflammatory CNS disease as described here occurs usually, but not exclusively, in patients with longstanding seropositive disease and considerable deformities. Not all patients with inflammatory CNS disease have subcutaneous nodules.

When performed, CSF examination reveals a raised protein content and a modest degree (or no) pleocytosis. Imaging has been helpful in a few cases by showing enhancement of meningeal structures. In the reported cases, vasculitis has never been discovered by angiography. In fact, the introduction of new imaging techniques has somewhat simplified making the diagnosis of cerebral vasculitis. These new techniques have

stimulated interest in cerebral vasculitis but have not increased the publication of new cases of rheumatoid vasculitis, and this casts some doubt on the entity 'rheumatoid cerebral vasculitis'. Meningeal rheumatic nodules are sometimes discovered at autopsy in patients without any neurological manifestations.

3. NORMAL PRESSURE HYDROCEPHALUS AND RHEUMATOID ARTHRITIS

Normal pressure hydrocephalus is characterized by dementia, unstable gait, and, urinary incontinence, and can be treated by ventriculo-peritoneal shunting. It was described by Rasker et al. in six patients with RA[46]. The relation between the two diseases, if any, remains unclear. In 1995, Markusse et al, reported on two further possible cases and suggested that it might be caused by obstruction of CSF absorption by chronic meningitis[48]. The authors observed improvement in their patients upon treatment with corticosteroids, and considered this as support for their hypothesis. In established and published cases of 'rheumatoid meningitis', normal pressure hydrocephalus has so far not been observed and reported.

4. RHEUMATOID ARTHRITIS OF THE CERVICAL SPINE .AND THORACOLUMBAR SPINE.

Epidemiology

Cervical spine lesions in patients with long-standing RA often form a point of great concern. Two years after the diagnosis of RA has been established, 10% of patients already show a mild degree of one of the different forms of cervical rheumatoid subluxations[53]. After approximately 10 years, one third of the patients have a form of cervical subluxation, and after mean disease duration of 15.7 years, the prevalence of cervical subluxation is 52%, as was shown in a population-based study in Finland. The

severity of the neck lesions correlates with the degree of erosion of metacarpo- and metatarsophalangeal joints. In contrast to cervical rheumatoid arthritis, thoracic arthritis rarely causes subluxation.

The reason for the excessive vulnerability of the cervical spine is not definitely clarified, but two factors are likely to play a significant role: the extreme mobility of the cervical spine and the heavy load it has to carry. It is of interest that the protective effect of hemiplegia on the development of rheumatoid joint lesions is explained by the decreased use of the joints on the same side of the body[57].

Destructive changes

Destructive changes occur in particular at the atlanto-occipital and atlanto-axial levels and to a lesser degree in the sub axial cervical segments. At each cervical segment, from the atlanto-occipital level downward, there are two lateral synovia-lined joints. The dens has, in addition, a small synovia-lined joint with the anterior arch of the atlas and another one with the strong transverse ligament that covers the dens at the posterior side[59]. This transverse ligament prevents posterior movement of the odontoid process towards or against the spinal cord during flexion of the cervical spine. From C2 downward there are small synovia-lined joints between the lateral edges of the cervical vertebrae. All these synovia-lined joints, as well as nearby ligaments, cartilage, and bone, may become affected and destroyed by the inflammatory rheumatoid process[60]. This may result in abnormal mobility and some degree of subluxation of cervical vertebrae, which potentially endangers the spinal cord.

Bulbo-myelopathy and radiculopathy

The neurological manifestations are in broad outline similar to other cranio-vertebral

syndromes. Displacement of vertebrae may narrow the space available for the radices in foramina intervertebralia, for the spinal cord in the spinal canal, and for the medulla oblongata in the foramen magnum. Compression of nervous structures may be intermittent, as in patients with reducible AAS, or permanent, as in most vertebral subluxations. Neurological symptoms and signs may therefore be intermittent also, though they are mostly definite.

Neurological evaluation of handicapped, deformed patients with long-standing rheumatoid arthritis and atrophy of peri-articular muscles is not easily performed. This is reflected by the descriptions in the literature on the neurology of the cervical spine lesions, which are usually put in very general terms[62]. Spinal cord compression develops only in a small minority of patients, after many years or even decades. Winfield et al followed a group of 100 patients from the first year after RA had been diagnosed. At the end of a 10 year period, one patient had developed cervical myelopathy.

Five forms of cervical subluxation

1. Anterior atlanto-axial subluxation (AAS) is caused mainly by laxity and destruction of the transverse ligament. The distance between the posterior side of the atlas and the anterior side of the odontoid process (normal less than 3 mm) is increased, and the diameter of the vertical canal (normal 18-26 mm) is decreased. At flexion of the neck, AAS increases (reducible AAS). This is the most frequent form of cervical subluxation.
2. Posterior AAS is due to severe erosion or fracture of the odontoid process that allows the atlas to move backward. This form of subluxation is uncommon.
3. Atlanto-occipital impaction (AAI) or vertical subluxation happens when the cranium descends on the cervical spine and the odontoid process moves upward through the

foramen magnum (normally, the odontoid process is below the foramen magnum), due to destruction of bone and cartilage at the occipito-atlanto and atlanto-axial joints. Authors use different criteria for AAI and the figures for its prevalence vary accordingly. It is probably the second most frequent form of cervical subluxation after AAS, and occurs after a longer period of disease than AAS. AAI has a stabilizing effect on AAS due to loss of mobility in the atlanto-axial joints.

4. Lateral AAS is due to unilateral or asymmetrical joint disease and destruction of the lateral mass of the atlas at that side. Patients show rotational tilting of the head towards the affected side.

5. Sub axial subluxation is due to intervertebral joint lesions and weakening of ligaments. Sub axial subluxation is held to be present when there is displacement of adjacent vertebral bodies of more than 3.5 mm as measured from the posterior side of the bodies. Sub axial subluxation tends to become more severe by fixation of the two upper cervical vertebrae, either by AAI or by operation. Long-standing cervical RA may occasionally result in progressive kyphosis from C2-C7, with compensatory lordosis at the craniocervical junction.

Neurological symptoms and signs in patients with cervical subluxations

1. In comparison to the degree of the cervica1 abnormalities and the evidence of bulbospinal compression, neurological signs are commonly less marked than one would expect. Symptoms and signs of the spinal cord and radiculi are much more frequent than bulbar syndromes and cranial nerve lesions.

2. Myelopathy: disturbance of gnostic sensibility is more frequent than of vital sensibility. Some patients have unilateral or bilateral astereognosis of the hands.

Lhermitte's sign may be present. Pyramidal changes include raised tendon reflexes with positive Babinski reflexes, spasticity, and muscle weakness in that order. Disorders of bladder and bowel motility are not rare.

3. Radiculopathy: severe pain in the occipital region presumably of radicular origin is relatively frequent.

4. Bulbar syndromes and cranial nerve lesions: dysphagia and dysarthria, vertigo, fainting, cerebellar signs, symptoms of Cr.N V, IX, X, XII, VII and rarely III, IV and VI. Obstructive hydrocephalus and secondary inappropriate antidiuretic hormone secretion have been reported.

BULBAR SIGNS

The hypoglossus, glossopharyngeus, and the vagus nerves were the most frequently affected cranial nerves, but one of the patients of Menezes *et al.* had loss of pain and touch in the distribution of the trigeminal nerve and another even had facial diplegia. In the group of Rana *et al,* eight of 41 patients with AAS had trigeminal sensory neuropathy. Toolanen determined the cutaneous threshold for the face in patients with AAS and AAI due to RA, and discovered changes in the ophthalmic and maxillary divisions of the trigeminal nerve but not in the mandibular division, presumably due to lesions in the trigeminal spinal tract. Obstructive hydrocephalus was reported in three cases, and was associated in one with secondary inappropriate antidiuretic hormone secretion. Symptoms of dysphagia and dysarthria of uncertain origin were present in 41 (respectively 35) of 186 patients operated for either AAS or AAI.

MYELOPATHY

Menezes *et al.* found hyperreflexia with positive Babinski signs in 36 of their 45 neurologically symptomatic patients with AAI. The authors had difficulty in adequately evaluating the strength of their patients. Posterior column sensory disorders were frequent, but hypalgesia was unusual. Nakano et al also found weakness in patients with hyper-reflexia and Babinski signs. Astereognosis of the hands was a feature of 18 of these 32 patients. Other sensory disturbances including hypalgesia were often present. Sixteen patients had bladder and/or rectal sphincter

dysfunction. Lhermitte's sign was present in 35 of 186 patients with myelopathy.

5. MYASTHENIA GRAVIS AND RA

MG is often associated with other auto immune diseases. The RA prevalence in patients with MG varies in different studies. It is according to Oosterhuis et al, from 0-10%. MG may be induced by treatment with penicillamine.

6. MUSCLE ATROPHY, MYOPATHY AND MYOSITIS.

Muscular strength and endurance in RA are, in general, less than in a control population, and patients have less muscle volume. These changes are conceived to be due to factors related to the inflammatory process and to inactivity. Muscles around arthritic joints may become obviously atrophic; this is one of the most common features of RA. Miro et al showed that proximal weakness is due to either myositis (DM or PM) or to an unwanted effect of medication (corticosteroids, D-Penicillamine, Chloroquine). The association of RA and inclusion body myositis (IBM) has been reported.

7. **NEUROPATHY IN RHEUMATOID ARTHRITIS.**

The most acceptable classification of Rheumatoid neuropathy is as follows.

1. **ENTRAPMENT NEUROPATHY**
    a. Carpal tunnel syndrome
    b. Tarsal tunnel syndrome.
    c. Posterior interosseus nerve entrapment
    d. Other nerves.
2. **NON-ENTRAPMENT NEUROPATHY.**
    a. Sensory neuropathy
    b. Motor neuropathy.
    c. Sensorimotor neuropathy
    d. Mononeuropathy
    e. Mononeuropathy multiplex.

NON-ENTRAPMENT NEUROPATHY.

EPIDEMIOLOGY:

Sensory and sensorimotor neuropathies do not often produce management problems in RA and for that reason the epidemiology of these disorders is not fully elucidated yet. Conn and Dyck[61] detected 25 cases of symptomatic peripheral neuropathy in a survey of 2162 RA patients all seen in Mayo clinic in 1971. The findings of Bekkelund et al[63] concerning nerve conduction in 52 women with seropositive and erosive RA and the lack of any evidence of neuropathy in this group support the view that peripheral neuropathies are infrequent. On the other hand Fleming et al [64], in a large longitudinal investigation of extra-articular features during the first five or six years after onset of RA, diagnosed distal sensory and distal motor neuropathies in 18 of 102

patients. Distal sensory neuropathy was more frequent than sensorimotor or motor neuropathy. This confirmed previous observations by Pallis and Scott [65], Chamberlain and Bruckner (1970), and Weller et al (1970) indicating that a relatively mild sensory neuropathy could be distinguished from severe forms with motor and sensory symptoms.

CLINICAL FEATURES AND COURSE.

Mild sensory neuropathy is stated to recover mostly spontaneously[67] and to occasionally become severe and sensorimotor[61]. Some of the more severe sensorimotor polyneuropathies present at onset as mononeuritis multiplex. In such cases, the patient complains suddenly about pain and dysaesthesia in the course of a peripheral nerve at one of the lower limbs and feet or more rarely at one of the hands and underarms. Weakness develops, thereafter, within hours or days. Gradually more nerves become involved and the clinical picture becomes symmetrical. This type of rheumatoid peripheral neuropathy is caused by vasculitis of small or medium-sized epineural vessels. The vascular changes resemble that of panarteritis nodosa.

In a retrospective investigation, Puechal et el (1995)[71]studied the clinical features of 32 patients with RA, peripheral neuropathy, and vasculitis established by nerve or muscle biopsy. Nearly 50% of the patients had a predominantly sensory neuropathy. Others had a sensorimotor polyneuropathy, a predominantly motor neuropathy, or mononeuritis multiplex, which demonstrated that all these types of neuropathies could potentially be caused by vasculitis. It is of interest that in a retrospective investigation of 61 patients with RA and histologically proven vasculitis done by voskuyl et al(1996)[70], 12% had mononeuritis multiplex and 15% had distal sensory neuropathy. These observations indicate, but do not prove that all forms of neuropathy, including mild sensory neuropathy, may be caused by vasculitis. No less than 25% of the

patients of Puechal et al had a relapse after recovery of their neuropathy. Vasculitic neuropathy, in this study, was a feature of long standing seropositive RA with rheumatoid nodules; the range of RA disease duration was, however, wide. The five year survival rate of patients with rheumatoid vasculitis varies in different studies: in Puechal et al[71] it was 57% and in Voskuyl et al[70] it was 67%.

DIAGNOSIS AND MANAGEMENT

Patients with mild sensory neuropathy should be examined for evidence of vasculitis. There is a reasonable chance that vasculitis can be discovered by the presence of skin lesions[71]. Less frequent are kidney or GIT lesions. Nail fold infarcts and splinter haemorrhages are also due to vasculitis, but only of small arteritis. These are often present, but need no therapy as they tend to recover spontaneously. They should not be considered as signs in support of a vasculitic origin of neuropathy. On its own, mild sensory neuropathy requires regular careful control. The available data suggest that one should wait and see what happens, as spontaneous recovery seems to occur in at least some cases. When there is a progress towards a sensorimotor neuropathy or in cases of mononeuritis multiplex, invasive diagnostic methods should be used and aggressive therapy should be started without delay. Muscle biopsies are at least as often diagnostic as sural nerve biopsies and are to be preferred as they cause disagreeable sequelae less often than sural nerve biopsies. Patients with rheumatoid vasculitis and severe organ involvement are likely to benefit from prompt initiation of therapy with high dose corticosteroids and cytostatic agents[70]. Luqmani et al(1994)prefer, however, intermittent high dose pulses of cyclophosphamide, initially at two weeks intervals, with low dose oral corticosteroids as supportive therapy. With this strategy, remission is obtained within months,

following which maintenance therapy is required. However ideal medication for maintenance therapy is not available yet. Azathioprine does not sufficiently prevent relapses and low dose corticosteroids have too many side effects.

COMPRESSION NEUROPATHIES

CARPAL TUNNEL SYNDROME

Compression of median nerve in the carpal tunnel is frequently seen in RA. In their prospective longitudinal investigation of 102 patients of RA of recent onset, Fleming et al (1976)[72] registered median nerve compression in 52% of patients overall. Other authors reported slightly lower percentages. Patients complain about numbness and tingling in digits1 (thumb) to 4. Pain in the median nerve innervated part of the hand may irradiate up to the elbow and even higher. Neurological examination may reveal disturbance of skin sensibility in the area innervated by the median nerve. Weakness of the thumb opposition and abduction and atrophy of the abductor pollicis brevis may develop later on, but may not be easy to assess in RA patients. The laboratory technique that is used to confirm is comparison of sensory conduction from the fourth finger along the median nerve with sensory conduction from the same finger along the ulnar nerve[73]. Therapy is conservative when the complaints are slight and includes local injection of corticosteroids in case of active carpal synovitis. When the complaints are more severe or when there is evidence of neurogenic thumb weakness surgery is required.

CRITERIA FOR DIAGNOSIS FOR CARPAL TUNNEL SYNDROME:

The diagnostic criteria for CTS includes a distal motor latency more than 4.3 ms for median motor nerve; motor or sensory nerve conduction velocity less than 45m/s and of more than 0.5 ms latency difference in comparative test on the other side.

TARSAL TUNNEL SYNDROME

The tibial nerve may become compressed behind and below the medial side of the ankle where it passes under the flexor retinaculum. Clinical manifestations are infrequent and comprise pain, tingling, and numbness of toes and the soles[75]. The diagnosis requires electrophysiological confirmation. The tibial nerve divides in the tunnel in two or three branches. Not all these branches need to be compressed to the same degree. When only one of the branches is involved, differentiation is necessary of tarsal tunnel syndrome from plantar nerve compression distal to the tarsal tunnel, and additional nerve conduction studies which are not easy to perform are required[76].

FINGER DROP BY POSTERIOR INTEROSSEUS NERVE ENTRAPMENT

The motor branch of the radial nerve separates from the sensory branch at the level of the elbow and passes below the elbow between the superficial and the deep part of the supinator muscle. At the site of entrance in the supinator muscle, the nerve may be compressed by the fibrous arch of the superficial part of the supinator or by the extensor carpi radialis. It may be compressed, at a slightly higher level, by fibrous bands, which may form the radialis tunnel. In all these cases, the main symptom is very characteristic, and comprises inability to extend the fingers due to weakness of the extensor digitorum communis muscle and the extensor pollicis[77]. Wrist extension is usually preserved and sensibility remains intact. This can be confirmed by electromyography. In patients with RA, the nerve is compressed or stretched by bulging, proliferative elbow synovium, which is often palpable and best visualized by MRI[78]. Treatment with local intra-articular steroids, NSAIDS or both has been successful in several cases.

Surgical decompression is advised when medical treatment is unsuccessful.

COMPRESSION OF OTHER NERVES

Compression of nerves at other sites is possible but exceptional. All cases of mononeuropathy in patients with RA deserve accurate diagnosis, as they may in fact be the onset of mononeuritis multiplex.

NEUROPATHY SYMPTOM SCORE

Symptomatology: Foot/Lower Leg	yes	no	
Burning sensation	□ 2	□ 0	
Numbness	□ 2	□ 0	
Paraesthesia	□ 2	□ 0	□ pt.
Feeling of weakness (fatigue, exhaustion)	□ 1	□ 0	
Cramps	□ 1	□ 0	
Pain	□ 1	□ 0	□ pt.
Localisation			
Feet	□ 2		
Lower leg	□ 1		
Elsewhere	□ 0		□ pt.
Exacerbation			
Present at night	□ 2		
Present during day and night	□ 1		
Only present during the day	□ 0		
Patient is awakened from sleep by the symptoms	Score from □ 1 add		□ pt.
Symptom improvement when			
Walking Standing Sitting or lying down	□ 2 □ 1 □ 0		□ pt.
	Total score:		□

NSS:

3-4 = mild symptoms

5-6 = moderate symptoms

7-10 = severe neuropathic symptoms

* In each point column, the maximum score can be given only once.

NEUROPATHY DEFICIT SCORE

		Side	right	left
Ankle jerk				
Reflexes:	normal		□ 0	□ 0
	diminished		□ 1	□ 1
	absent		□ 2	□ 2
Vibratory sensibility				
(Normal values see Table 5)				
Measurement dorsal on big toe joint			right	left
	normal		□ 0	□ 0
	diminished/absent		□ 1	□ 1
Pain sensation				
Measurement on the dorsum of the foot			right	left
	normal		□ 0	□ 0
	diminished/absent		□ 1	□ 1
Temperature perception				
Measurement on the dorsum of the foot			right	left
	normal		□ ○	□ ○
	diminished/absent		□ 1	□ 1
		Total score: □		

NDS:

3-5 = mild neuropathic deficits

6-8 = moderate neuropathic deficits

9-10 = severe neuropathic deficits

FUNCTIONAL GRADING:

ACR CLASSIFICATION CRITERIA FOR FUNCTIONAL STATUS IN RHEUMATOID ARTHRITIS

Class I: Completely able to perform usual activities of daily living (self-care, vocational, and avocational)

Class II: Able to perform usual self-care and vocational activities, but limited in avocational activities

Class III: Able to perform usual self-care activities, but limited in vocational and avocational activities

Class IV: Limited ability to perform usual self-care, vocational, and avocational activities.

Self-care activities include dressing, feeding, bathing, grooming, and toileting. Avocational (recreational and/or leisure) and vocational (work, school, homemaking) activities are patient-desired and age- and sex-specific.

RADIOLOGICAL GRADING

RAU AND HERBORN MODIFICATION OF THE LARSEN METHOD.

Thirty two joints are evaluated: eight PIPS, two IP of the thumbs, 10 MCP, two wrists, and 10 MTP. The six stages are defined as follows: 0 = normal; 1 = soft tissue swelling and/or joint space narrowing/subchondral osteoporosis; 2 = erosions with destruction of the joint surface (DJS) <25%; 3 = DJS 26–50%; 4 = DJS 51–75%; 5 = DJS >75%. The score ranges from 0 to 160. In this modification the stages are described as a quantitative measure of the destroyed joint surface area and can therefore be applied more easily.

IMPORTANT STUDIES ABOUT RHEUMATOID NEUROPATHY:

The important studies that had been done about neuropathy in Rheumatoid arthritis are listed below as short abstracts.

PERIPHERAL NEUROPATHY WITH NECROTIZING VASCULITIS IN RHEUMATOID ARTHRITIS

Xavier Puéchal , Gerard Said, Pascal Hilliquin, Joel Coste, Chantal Job-Deslandre, Catherine Lacroix, Charles J. Menkès, Paris, France.

ABSTRACT

Objective. To examine the clinic pathologic features of the noncompressive neuropathies in rheumatoid arthritis (RA).

Methods. We studied 32 patients with RA and peripheral neuropathy whose nerve and/or muscle biopsy specimens exhibited necrotizing vasculitis. Morphologic analysis of nerve specimens included light and electron microscopy studies and teased fiber preparation. Survival was evaluated, and the prognostic values of clinical, biologic, and pathologic features were assessed by Cox proportional hazards model. A prognostic assessment based on the significant variables was devised to estimate the probability of survival of any individual patient.

Results. Epi and/or perineurial vasculitis was observed with the same frequency in the 17 patients with sensory and motor deficit and the 15 patients with sensory neuropathies and was associated with axonal degeneration of an average of 77.7% of the nerve fibers. The mean follow up was 7.2 years, and the overall survival rate at 5 years was 57%. A full prolonged remission of the vasculitis was observed in 53% of the patients relapse occurred in 25%. The factors correlated with mortality, in decreasing order of significance, were clinical cutaneous

vasculitis ($P = 0.0003$), neuropathy affecting 3 or 4 limbs ($P = 0.03$), and depressed level of C4 ($P < 0.05$). The prognostic assessment indicated a wide range of 5-year probabilities of survival, from <1% to 93%.

Conclusion. Necrotizing vasculitis is responsible for the different patterns of noncompressive neuropathies in RA, including mononeuritis multiplex and distal symmetric sensory or sensorimotor neuropathy. Cutaneous vasculitis, multifocal neuropathy, and depressed C4 level were the 3 independent variables which best predicted mortality. We propose a prognostic assessment according to these variables, to stratify patients to receive more aggressive or less aggressive therapy.

NEUROLOGIC COMPLICATIONS OF RHEUMATOID ARTHRITIS.

Rheum Dis Clin North Am. 1993 Nov; 19 (4):955-73

Chang DJ, ***Paget SA***. *Hospital for Special Surgery, New York Hospital, New York.*

Neurologic complications are common extraarticular manifestations of RA, involving both the peripheral and central nervous systems. Because RA patients suffer from pain, stiffness, and weakness, the detection of neurologic impairment is often difficult. Thus, close vigilance and thoughtful use of various diagnostic methods will help in the early diagnosis of cervical spine involvement, compression neuropathies, peripheral neuropathies, myopathies, and central nervous system involvement. Prompt and timely interventions may prevent permanent neurologic sequelae.

THE FREQUENCY OF CARPAL TUNNEL SYNDROME IN PATIENTS WITH RHEUMATOID ARTHRITIS

Mehmet Ufuk Aluclu, M.D., *Department of Neurology Turkey*

Abstract

Objective: Rheumatoid Arthritis (RA) may be associated with vasculopathy, peripheral, autonomic and entrapment neuropathy. In this study, carpal tunnel syndrome (CTS) in patients with RA was investigated.

Subjects and Method: 40 adult patients (totally eighty hands) with RA according to the revised criteria of American College of Rheumatology and 20 healthy volunteers (totally forty hands) for control group were included into the study. Nerve conduction velocity was performed to the both groups.

Results: Carpal tunnel syndrome (usually in sensorimotor axonopathy form) was determined in 20 hands (25%) of the patients with RA but it was not found in the control group. The three hands had minimal CTS (3.75%), five hands had mild CTS (6.25%), five hands had moderate CTS (6.25%) .

Conclusions: In this study, the prevalence of CTS in patients with RA may be high. We consider that treatment of CTS by medical and/or surgery methods in RA patients will decrease complaints and increase life quality. Therefore, we recommend that an electroneurophysiologic examination should be performed in all patients with RA as routine diagnostic procedure.

TARSAL TUNNEL SYNDROME AND PERIPHERAL NEUROPATHY IN RHEUMATOID DISEASE

Annals of the Rheumatic Diseases, 1983, 42, 128-131, Loius Mcguigan, David Burke, Anthony

Fleming. The Prince Henry Hospital, Sydney , Australia

SUMMARY

Thirty patients with classical or definite rheumatoid disease (RD) with foot pain and radiologically demonstrated erosions were studied electro diagnostically to ascertain the frequency of the tarsal tunnel syndrome and peripheral neuropathy. Four patients (13.3%) had evidence of the tarsal tunnel syndrome. The electrical abnormalities were mild and unassociated with specific clinical features. Two patients (66 %) had evidence of sensory peripheral neuropathy. There may be an appreciable frequency of clinically unsuspected tarsal tunnel syndrome in RD.

INTERSTITIAL LUNG DISEASE AND NEUROPATHY AS PREDOMINANT EXTRA-ARTICULAR MANIFESTATIONS IN PATIENTS WITH RHEUMATOID ARTHRITIS: A PROSPECTIVE STUDY

Anurag Bharadwaj, Nigil Haroon, Department of Immunology-Rheumatology, Kasturba Medical College, Manipal, India

SUMMARY

Background: Rheumatoid arthritis (RA) patients with extra-articular manifestations (ExRA) have a severe course of the disease and higher mortality. Indian patients are considered to have a low prevalence of ExRA. We prospectively assessed ExRA in patients with rheumatoid arthritis from southern India.

Material/Methods: 140 RA patients were qualified for the study. Patients with confounding factors were excluded. A detailed history and clinical examination was performed. Two independent investigators made a thorough search with relevant investigations for ExRA, according to well-defined criteria. Results: At least one ExRA was present in 36 patients (25.7%). The predominant ExRA (9.29%) was Interstitial Lung Disease (ILD). 12 patients had neuropathy (8.57%). 5 patients had eye involvement, while 3 had cutaneous vasculitis. 4 patients had rheumatoid nodules, and 1 had amyloidosis. The median age at diagnosis and duration of disease were significantly higher in patients with ExRAs than in those without. Deformities and the use of steroids were more common in the ExRA cohort.

Conclusions: The present study shows a high prevalence of ILD and neuropathy as ExRAs in our population. A more extensive investigative protocol is warranted for picking up milder presentations of these serious manifestations.

NEUROPATHY IN RHEUMATOID ARTHRITIS

Nadkar MY, Agarwal R, Samant RS, Chhugani SJ, Idgunji SS, Iyer S, Borges NE

J Assoc Physicians India 2001 Feb.:217-20.

BACKGROUND: Paucity of Indian literature on rheumatoid neuropathy creates a lacuna in the critical evaluation and discussion of the subject. We did this study to find out the incidence and pattern of neuropathy and to correlate it with disease parameters and other extra-articular involvement.

MATERIAL AND METHODS: We studied 31 patients of rheumatoid arthritis (RA) classified by ACR criteria. Electromyography and nerve conduction studies (EMG/NCV) were done in all the patients apart from routine laboratory and radiological investigations. Electrocardiograph (ECG), pulmonary function tests (PFT) and ophthalmological examinations were also carried out to ascertain extra-articular involvement.

RESULTS: Ten out of 31 RA patients had neuropathy of which five each were overt and sub clinical respectively. Only one patient had entrapment neuropathy. Four of the ten patients had pure motor neuropathy whereas the other six were sensori-motor neuropathies. Four patients had mononeuritis multiplex and five had symmetrical peripheral neuropathy. Nine of the ten neuropathic patients had RA for more than 2 years. Seven patients had other extra-articular features along with neuropathy.

CONCLUSIONS: One-third of patients with RA have evidence of neuropathy. Disease parameters such as activity, rheumatoid factor and functional and radiological grade do not correlate with neuropathy. Non-entrapment sensori-motor type of neuropathy is the most common type.

CRANIAL AND PERIPHERAL NEUROPATHY IN RHEUMATOID ARTHRITIS WITH SPECIAL EMPHASIS TO II, V, VII, VIII AND XI CRANIAL NERVES

Sherifa A. HAMED, Eman A. HAMED , Amal M. ELATTAR , Mohamed S. AbdeL RAHMAN and Nabila F. AMINE . Egypt.

Background: Cranial neuropathy in rheumatoid arthritis (RA) is relatively rare compared to the frequently reported peripheral neuropathy.

Methods: We investigated the occurrence of subclinical cranial and peripheral nerve involvement in 55 patients with RA.

Results: Patients had a mean age of 43.1 years and a mean duration of illness of 6.4 years. All patients presented with electrophysiological findings suggestive of peripheral neuropathy. In addition, 69.1% of them had entrapment neuropathies, in which carpal tunnel syndrome was the most common (54.6%). Sensorimotor neuropathy at sites other than usual entrapment sites was diagnosed in 70.9%, while bilateral distal sensory neuropathy in lower limbs was identified in 29.1%. Among cranial nerves examined, optic and vestibulocochlear neuropathies were common (29.1% of eyes and 40% of ears examined). Spinal accessory neuropathy was reported in 21.8% of records. Neither facial nor trigeminal nerves were affected. Electrophysiological characteristics of neuropathies were indicative of axon loss. Significant association was identified between neuropathy and patients' ages ($P < 0.01$), duration of the illness ($P < 0.001$), presence of rheumatoid nodules ($P < 0.001$) and disease stages ($P < 0.001$).

Conclusions: Our results indicate that cranial and non-compressive neuropathies are not uncommon in RA. This extends the pathologic disease spectrum. We do not confirm, but suggest the contribution of chronic immune-mediated vasculitis and/or neurotoxicity in RA neuropathies. Of clinical importance, subclinical neuropathy may never progress and/or be of clinical significance, which contradicts that of comparable diseases, such as systemic lupus erythematosus. Advances in genetics implicate a complex immune genetics which controls susceptibilities and adaptive molecular mechanisms as a culprit of phenotypical heterogenicity among related diseases.

SUBCLINICAL PERIPHERAL NERVE INVOLVEMENT IN PATIENTS WITH RHEUMATOID ARTHRITIS

B. Lanzillo, N. Pappone, C. Crisci, C. Di Girolamo, R. Massini, G. Caruso

Italy

 **ABSTRACT**

Objective: Clinical involvement of the peripheral nervous system is uncommon in rheumatoid arthritis (RA); the most common disorders are multiple mononeuritis, sensorimotor neuropathy, and entrapment neuropathy. This study was undertaken to investigate the occurrence of electro physiologically evident peripheral nerve involvement in RA patients without a clinical history of peripheral nerve involvement.

Methods: Forty RA patients were examined neurologically and electro physiologically, and

sural nerve biopsies were performed in 4. Results: No patient reported symptoms or signs of peripheral nerve involvement. Twenty-six patients (65%) exhibited electro physiologic findings consistent with a sensorimotor neuropathy (in 2 of them a carpal tunnel syndrome was also present), while 3 patients showed isolated carpal tunnel syndrome. There was a moderate loss of myelinated fibers in 3 of the 4 nerve biopsy samples, and all showed an increased number of endo- and perineurial vessels and some signs of axonal degeneration. **Conclusion:** Patients with RA may have electro physiologic and histologic findings of peripheral nerve damage, even in the absence of clinical evidence of peripheral nerve involvement.

THE ELECTRONEUROPHYSIOLOGICAL EVALUATION OF RHEUMATOID ARTHRITIS PATIENTS

A. Sivri and F. Güler-Uysal , Turkey

ABSTRACT

In Rheumatoid Arthritis (RA), one clinical hallmark of the vasculitis is the appearance of neurological findings. However, it is often difficult to diagnose these slight or early neuropathies and the study of the peripheral neuromuscular system is often made difficult by symptoms resulting from pain in the joints, and limitations of movement. It is nevertheless often possible, by means of electroneuromyography to show objectively the existence and distribution of even sub clinical neuropathies. In order to evaluate the neurophysiological functions of RA patients by means of the peripheral nerve conduction and somatosensory evoked potential studies, 33 RA patients and 20 healthy controls were included in this study.

Two (6%) patients were found to have carpal tunnel syndrome, while 6 (18%) patients had mononeuritis multiplex. Delayed N12, N13, N1 and P1 latencies were detected in 6 (18%) of 33 RA patients suggesting central nervous system involvement with intact peripheral nervous system. Our results confirm earlier observations that symptoms of neuropathy are fairly common in cases of RA without there being any clear correlation with any clinical variable. Therefore, the inclusion of an electroneuro-physiologic examination of the RA patients is recommended in routine diagnostic procedure.

SENSORY NEUROPATHY IN RHEUMATOID ARTHRITIS: AN ELECTRONEUROGRAPHIC STUDY.

Scand J Rheumatol. 1981; 10(2): 81-4 .Lang AH, Kalliomaki JL, Puusa A, Halonen JP.

In a selected series of twenty-three RA patients, aged from 23 to 56 years, mean 41, the neurophysiological functions of six sensory nerves were measured and the results were correlated with clinical and laboratory data. Significant changes in the functions of one or more nerves were found in 10 patients, 2 of whom had no symptoms of clinical neuropathy. There was a highly significant correlation between neurophysiological symptoms and clinical neuropathy symptoms, although the combination of the clinical and electrophysiological findings was variable. On the other hand, there was no significant correlation between neurophysiological/neurological findings and clinical/laboratory data (age, sex, duration of disease, stage of disease, rheumatoid factor and erythrocyte sedimentation rate). Manifest or sub-clinical mono-neuropathies in n. medianus were found in 5 patients. In the light of these results it would seem in order to recommend the inclusion of an electro-neurophysiological examination of the median nerves of RA patients in routine diagnostic procedures.

LATENT NEUROPATHY IN RHEUMATOID ARTHRITIS ELECTROPHYSIOLOGICAL STUDY OF 45 CASES

*Minerva Med. 1982 Mar 3; 73(9); 473-8 .**Canesi B, Colombo S, Marobbio C, Rossi AF.*

Thirty (88.2%) of thirty four patients with rheumatoid arthritis showed evidence of latent neuropathy, as judged by the following tests: measurements of motor and sensory conduction velocity; analysis of single motor units at various sites and under different conditions. All patients demonstrating electrophysiological signs of involvement of nervous functions showed no clinical signs of peripheral neuropathy. On the basis of the present results it is proposed that neurophysiological alterations could depend on a widespread (immunologically mediated) injury of the axonic membrane.

MATERIALS AND METHODS

This study was done at the Institute of Neurology, Government General Hospital, Chennai in collaboration with the Department of Rheumatology.

TYPE OF STUDY

This study was designed as a non randomized prospective study.

STUDY PERIOD.

The study was conducted during the period between February 2006 and March 2007.

STUDY POPULATION.

Patients who came to the Rheumatology Outpatient Unit and those of the referred rheumatological cases, with neurological complaints, were taken up for this study. Patients were selected based on Inclusion and Exclusion criteria.

INCLUSION CRITERIA

Patients with Rheumatoid arthritis who strictly fulfilled the 1988 revised criteria ACR classification criteria for Rheumatoid arthritis. Both, the patients with and without symptoms suggestive of neuropathy were included.

EXCLUSION CRITERIA

Patients with diabetic mellitus, hepatic/renal diseases, leprosy, chronic drug abuse or any other known causes of neuropathy were excluded.

STUDY PROTOCOL.

Clinical data was collected from patients in a systematic manner and noted down in a standardized proforma.

Detailed history regarding duration and progression of rheumatoid arthritis was noted. Functional impairment was graded as per ACR criteria. History suggestive of neuropathy with its duration, symptoms, distribution, onset, progression and relation to therapy were also noted. Complete neurological examination including power, tone, sensations and reflexes was done in all the patients. Each patient was given a Neuropathy Symptom Score (NSS) and Neuropathy Deficit Score (NDS) score after the clinical examination. Other extra-articular manifestations, if any were also taken down.

Following investigations were carried out in all patients. The list included Complete Blood Count, ESR, CRP, RF, FBS, blood urea, creatinine, calcium, phosphorus, LFT, HIV and radiography of the affected joints. ECG, PFT, ophthalmological evaluations were done whenever necessary to look for extra-articular manifestations.

Electro diagnostic protocol, as recommended by AAEM was used. Neurophysiological studies were performed by RECORDERS & MEDICARE SYSTEMS EMG. EP MARK – II, EMG machine, a 4channel electrophysiological device. Nerve conduction studies in the upper limbs included sensory and motor conductions of ulnar and median nerves. In the lower limbs motor conductions in peroneal and tibial nerves & sensory conduction in sural nerve were done in all the patients. The temperature of the room was maintained at 22-24ºC during all processes. Standardized nerve conduction techniques were used. Conventional methods using surface electrodes for motor conduction and ring electrodes for sensory conduction were used. Latencies were measured from initial deflection of action potential in motor and at peak of negative spike in sensory studies. Amplitude represented distance between isoelectric trace and

negative peak in sensory and peak to peak in motor conduction studies. Standardized criteria were used to diagnose carpal & tarsal tunnel syndrome.

STATISTICS

All results were presented as mean ± S.D. The Chi Square test was used for statistical analysis. The level of significance was set at P value of 0.05.

RESULTS

Total number of patients who fulfilled the inclusion and exclusion criteria was 59. Out of them 14(23.72%) patients had features of neuropathy.

The mean age of the 59 patients was 38.97yrs (range 20 to 67yrs).The mean age of patients

with neuropathy was however 42.78yrs (range 26 to 67yrs).

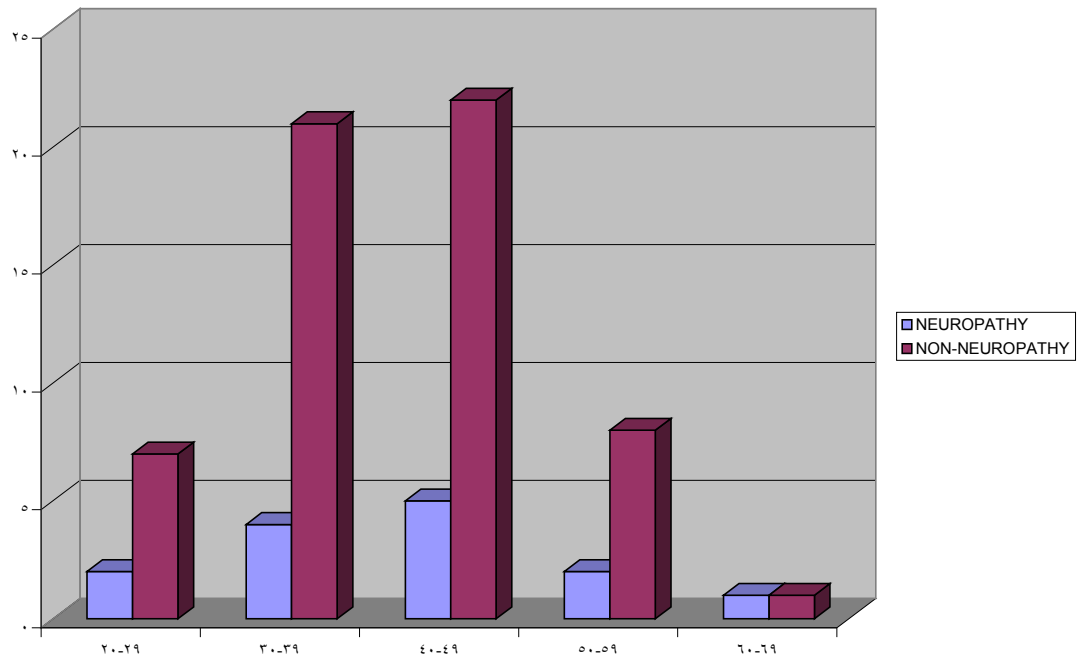
AGE IN YEARS	NO. OF PATIENTS	PERCENTAGE (%)
20-29	2	14.28
30-39	4	28.57
40-49	5	35.71
50-59	2	14.28
≥60	1	7.14

AGE RANGE	NEUROPATHY PRESENT	NEUROPATHY ABSENT	P VALUE
20-49	11	40	
50-70	3	5	0.3217

Only ten of the patients were males. The incidence of neuropathy was higher in males than females. Five out of ten (50%) and nine out of 49 (18.36%) had neuropathy.

CHART : 1 . AGE DISTRIBUTION

AGE DISTRIBUTION



SEX	NO. OF PATIENTS	PERCENTAGE (%)
MALE	5	35.71
FEMALE	9	64.28

SEX	NEUROPATHY PRESENT	NEUROPATHY ABSENT	P VALUE
MALE	5	5	
FEMALE	9	40	0.03206

Duration of RA ranged from 6 months to 15 yrs.Duration of RA was ≤2 in four (28.57%) patients with neuropathy; whereas five (35.71%) had disease duration of 3-5 years and four (28.57%) had disease for more than 5 years.

DURATION IN YRS	NO. OF PATIENTS	PERCENTAGE (%)
≤2	4	28.57
3-5	5	35.71
6-10	3	21.42
>10	2	14.28

CHART 2 : SEX DISTRIBUTION – I

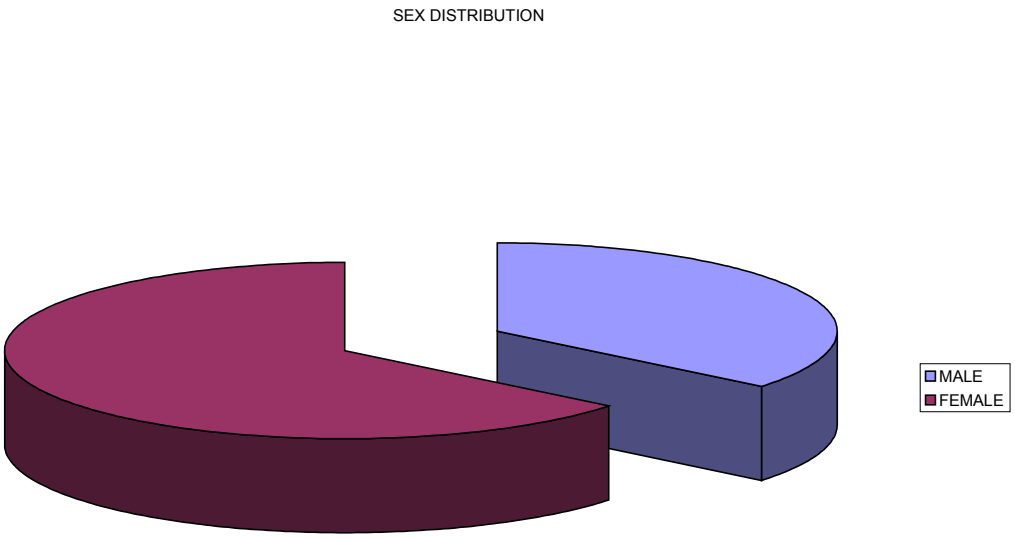
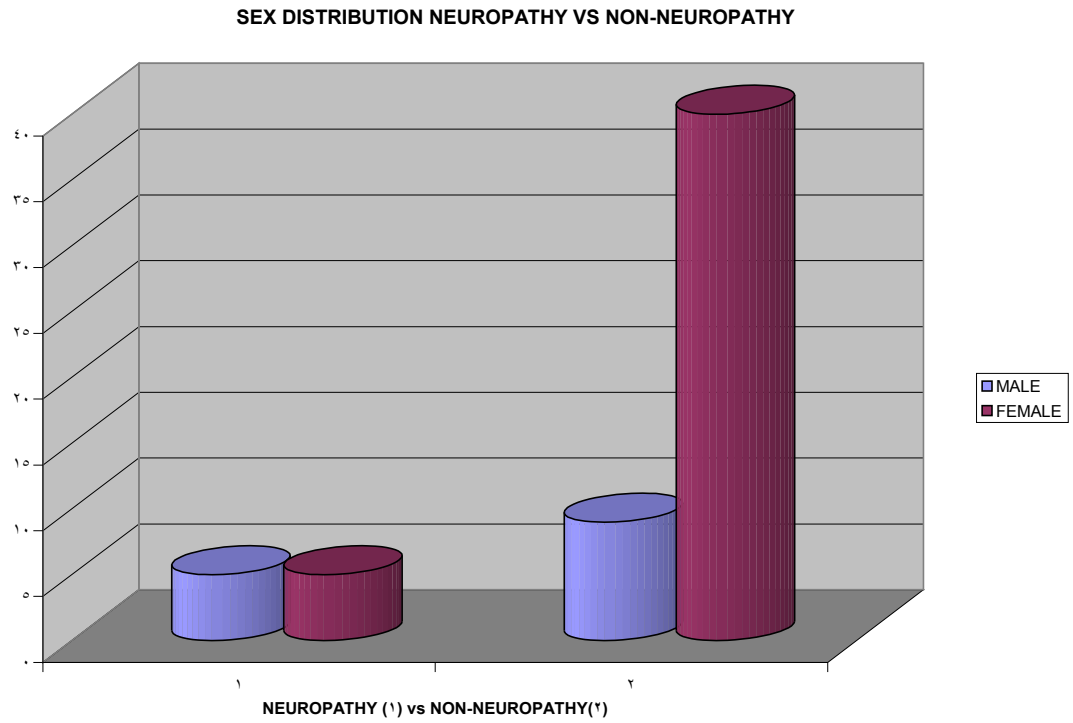


CHART. 3. SEX DISTRIBUTION – II



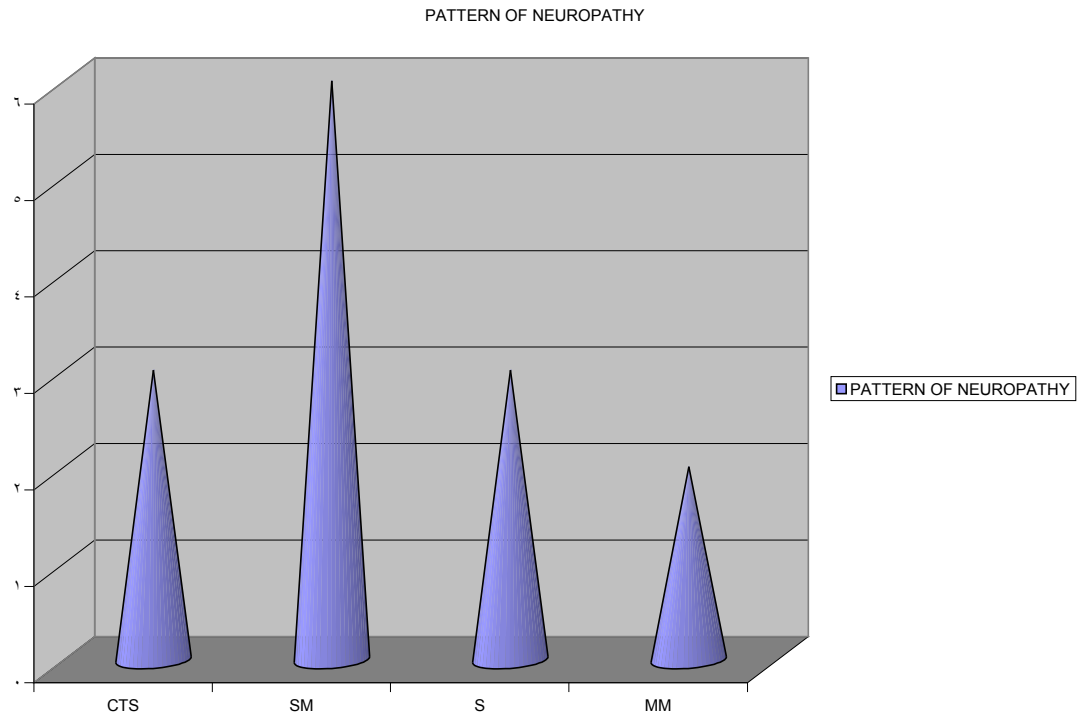
DURATION	NEUROPATHY PRESENT	NEUROPATHY ABSENT	P VALUE
≤5	9	36	
6-15	5	9	0.2292

Out of the fourteen patients with neuropathy, only three (21.42%) were sub clinical. Rest (78.57%) had overt neuropathy.

About the pattern of neuropathy, three (21.42%) had entrapment neuropathy and the remaining eleven (78.57%) had non entrapment neuropathies. Among the eleven patients with non entrapment neuropathies six (42.85%) had sensorimotor type of neuropathy; three (21.42%) had pure sensory neuropathy; one had mononeuropathy and another had mononeuropathy multiplex respectively. All the three entrapments were in the **carpal tunnel.**

PATTERN	NO.OF PATIENTS	PERCENTAGE (%)
ENTRAPMENT N	3	21.42
NON-ENTRAPMENT	11	78.57
1.SENSORIMOTOR	6	42.85
2.SENSORY	3	21.42
3.M. MULTIPLEX	2	14.28

CHART . 5. PATTERN OF NEUROPATHY.



All the non entrapment neuropathies were of **axonal type**.

RA functional class was I or II in five (35.71%) and III or IV in nine (64.28%) patients.

Radiological grading was I, II, III, and IV in six, four, three and one patient respectively.

Rheumatoid factor was positive in ten (71.42%) patients with neuropathy, while in four (28.57%) it was negative.

R.F	NO. OF PATIENTS	PERCENTAGE
POSITIVE	10	71.42
NEGATIVE	4	28.57

C reactive protein reflecting the activity of the disease as found to be raised in eleven (78.57%) patients with neuropathy.

CRP	NO. OF PATIENTS	PERCENTAGE
POSITIVE	11	78.57
NEGATIVE	3	21.42

Erythrocyte sedimentation rate was raised in twelve (85.71%) patients, with an average of 60.25mm at the end of first hour.

CHART . 4. OVERT VS COVERT NEUROPATHY

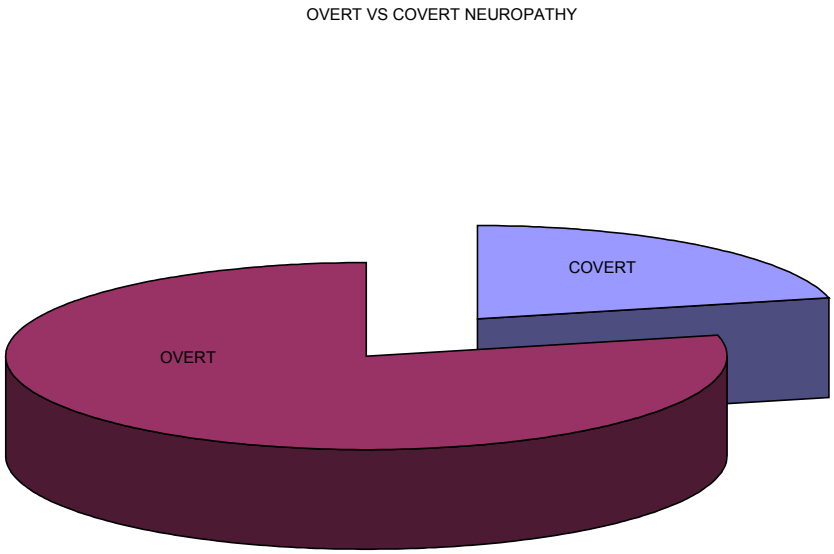


CHART. 6. DURATION OF DISEASE

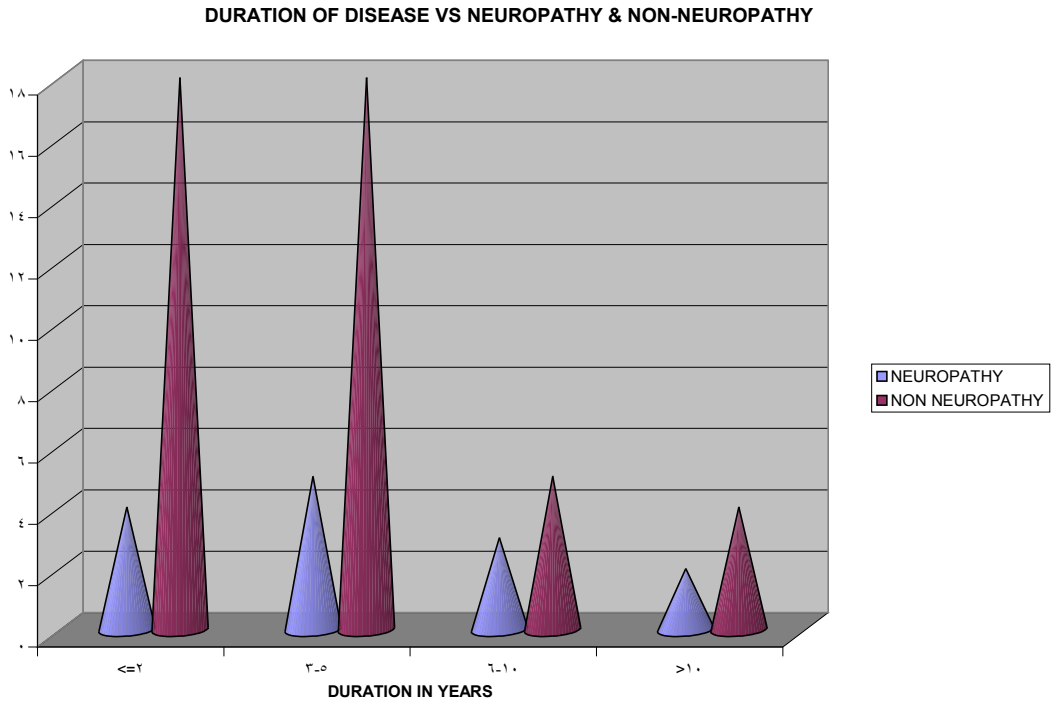


CHART. 7. EXTRA-ARTICULAR MANIFESTATIONS.

EXTRA-ARTICULAR MANIFESTATIONS

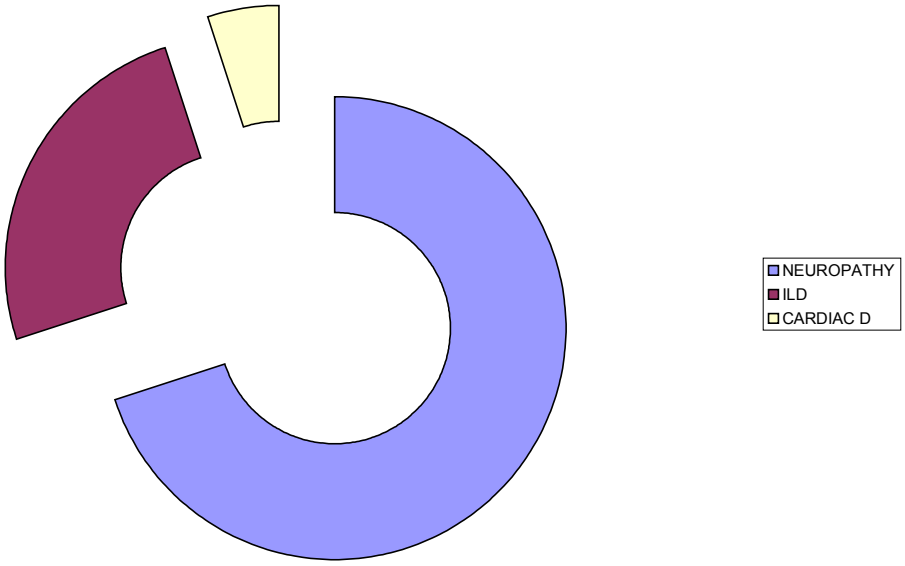


CHART. 8. RHEUMATOID FACTOR VS NEUROPATHY.

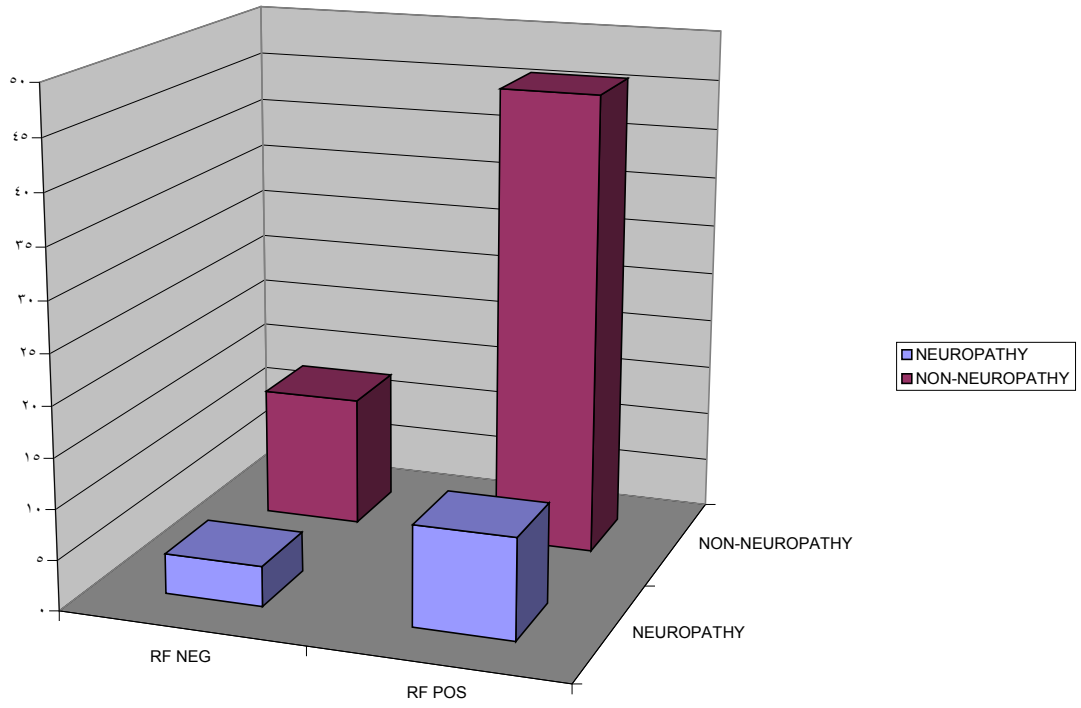


CHART. 9. CRP VS NEUROPATHY

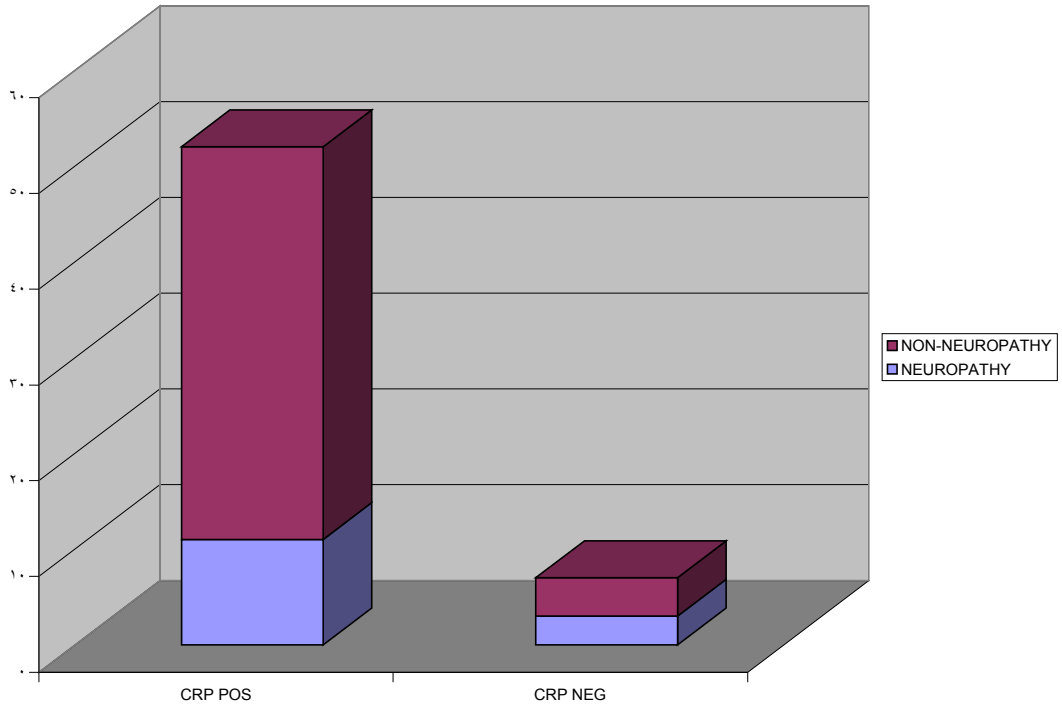
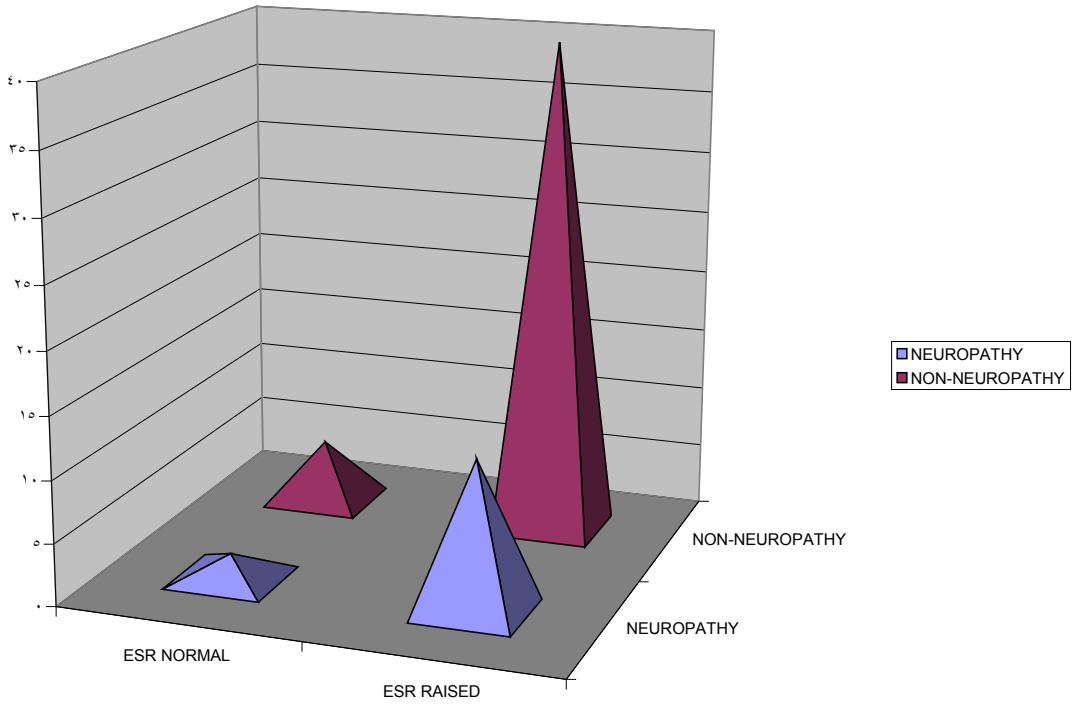


CHART. 10. ESR VS NEUROPATHY.



ESR	NO. OF PATIENTS	PERCENTAGE
RAISED	12	85.71
NORMAL	2	14.28

PARAMETERS	NEUROPATHY PRESENT	NEUROPATHY ABSENT	PVALUE
CRP	11	3	0.205578
RAISED ESR	12	2	0.74966
RA FACTOR	10	4	0.49841

Out of the 59 patients, sixteen (27.11%) had extra-articular manifestations which included fourteen (23.72%) with neuropathy, five (8.47%) with pulmonary affection as judged by PFT and one (1.69%) had cardiac involvement. Neuropathy with pulmonary involvement was present in three patients and only one patient had all three system affection.

All the patients with neuropathy had received aspirin. Three had received methotrexate and one had prednisolone.

DISCUSSION

Internationally, the overall incidence of neuropathy in Rheumatoid arthritis in different studies had varied from 40% to 70%[65,70]. In an Indian study done in 1991 by Kar et al[86], the incidence was 20%. Nadkar et al[84] published a study in 2001, where they quoted an incidence of 32%. In our present study, the overall incidence of neuropathy is 23.32%, which is quite comparable with the Indian studies.

In the Kar et al study[86], the incidence of overt neuropathy was only 5.7% with the rest being sub clinical involvement. Nadkar et al[84] showed equal (50%) incidence of overt and sub clinical neuropathy. But our study shows high incidence of overt neuropathy (78.57%).

The incidence of entrapment neuropathy is reportedly more common than non-entrapment variety, comprising 50-90% of total neuropathy in RA in various studies while non-entrapment neuropathy is reported in 10-50% of the patients with rheumatoid neuropathy[64]. But in Nadkar et al[84] study the incidence of entrapment neuropathy was very low (10%). Our study also shows similar low incidence of entrapment neuropathy. There is no apparent reason for the low incidence of entrapment neuropathy in our study.

It is believed that the mean age at onset of neuropathy does not correlate with the presence, severity or the type of neuropathy. It has been reported to vary widely from less than 40 years to more than 70 years[2,14]. In this study, patients having rheumatoid neuropathy have ages ranging from 26 years to 67yrs, with an average of 42.78yrs.

Most series report that male patients of RA have a higher incidence of rheumatoid neuropathy than female patients[39, 64, 72, 86]. The male to female ratio in various reports is found to range from

0.5:1 to 2.6:1, with most studies having a ratio of around 1:1.This is in contrast to the general population of RA where females predominate by at least 2:1. This male preponderance of rheumatoid neuropathy is also true of other extra-articular manifestations of RA[86]. In this study also, male rheumatoid patients are more susceptible to get neuropathy. In statistical analysis, male sex was found to be statistically correlated with the occurrence of neuropathy in RA.

Giovanni et al (2006)[60] had published in their study a significant correlation between occurrence of peripheral neuropathy and Neuropathy Deficit Score but not with the Neuropathy Symptom Score. In this study too, there is a significant correlation between NDS and occurrence of neuropathy, while the NSS did not show any correlation.

Several authorities have reported that extra-articular features including neuropathy are related to the duration of disease. The average duration of RA before the development of neuropathy has been found to vary from 4.5-12 years with the duration of RA ranging from 3 months to 47 years[39, 64, 72, 86]. In most of the series neuropathy was observed in patients with duration of disease more than 2 years[39, 72]. In the present study, patients having rheumatoid neuropathy had RA ranging from 6months to 15 years, with an average of 3.84yrs.

The most widely held view has been that neuropathy may be related to the severity of RA. Gordon[58] reported that the highest level of functional impairment and highest frequency of severe articular disease was found in patients with one or more extra-articular features. But, in Kar et al[86] study there was no correlation between poor functional class and severe disease radiologically, with the occurrence of neuropathy in RA. In this study too there is no statistical correlation between occurrence of neuropathy and severe disease functionally as well as radiologically.

It has been reported that 77-100% of patients with rheumatoid neuropathy are seropositive.

Agarwal et al[2] found that 10% of patients with rheumatoid vasculitis were seronegative. McCombe[87] in his study, found significantly higher titers of RF In this study, out of 14 patients with neuropathy, 10 (71.42%) were seropositive while the remaining 4 (28.57%) were seronegative.

In most series it is well documented that patients with rheumatoid neuropathy and rheumatoid vasculitis have a greater ESR at the time of examination. In this study, 12 patients had a high ESR. But both ESR and RF were not significantly correlated with rheumatoid neuropathy.

Gordon[58] reported presence of one extra-articular feature in 34% of patients and two or more extra-articular features in 42% of patients with rheumatoid arthritis. In the present study, out of 59 patients of RA, 1 patient had three extra-articular system involvement, three had 2 extra-articular system involved and 11 had only one extra-articular system involved.

After statistically analyzing all the variables, only male sex and NDS were found to be significantly correlated with the occurrence of neuropathy. NDS is a scale based on specific neurological examination whereas NSS is a score based on subjective neurological symptoms. Hence lack of correlation between NSS and neuropathy confirms that, in these patients discernment between neuropathic pain and arthritic pain may be arduous without careful neurological evaluation. And a significant correlation between NDS and neuropathy means that NDS should be incorporated in the initial evaluation of peripheral nerve involvement in Rheumatoid arthritis patients.

CONCLUSIONS

- One fourth of the patients with Rheumatoid arthritis had evidence of neuropathy.
- Non entrapment neuropathy was the predominant type of neuropathy among which sensorimotor type was the most common one.
- Among the disease parameters, only male sex and Neuropathy Deficit Score (NDS) were found to be significantly correlated with rheumatoid neuropathy.

BIBLIOGRAPHY

1. Turesson C, O'Fallon WM, Crowson CS et al. Incidence of extra- articular disease manifestations in a population-based cohort of patients with rheumatoid arthritis. Arthritis Rheum, 2000; 43(Suppl.9): S152
2. Agarwal V, Sachdev A, Lehl S, Basu S: Unusual hematological alterations in rheumatoid arthritis. J Postgrad Med, 2004; 50: 60–61
3. Bandyopadhyay SK, Bandyopadhyay R, Dutta A: Acquired pure red cell aplasia in a patient of rheumatoid arthritis and autoimmune hypothyroidism: a rarely reported association. J Indian Rheumatol Assoc, 2003; 11: 87–88
4. Turesson C, Jacobsson L, Bergstrom U: Extra-articular rheumatoid arthritis; prevalence and mortality. Rheumatology, 1999; 38: 668–74.
5. Erhardt CC, Mumford PA, Venables PJW, Maini RN: Factors predicting the prognosis in rheumatoid arthritis: An eight-year prospective study. Ann Rheum Dis, 1989; 48: 7–13
6. Felson DT. Epidemiology of Rheumatic diseases Koopman WJ. Arthritis and allied conditions. A textbook of rheumatology, 13th ed, pp 3-34. Baltimore: Williams and Wilkins.
7. Suzuki A, Ohosone Y, Obana M et al: Cause of death in 81 autopsied patients with rheumatoid arthritis. J Rheumatol, 1994; 21: 33–36
8. Hakala M: Poor prognosis in patients with rheumatoid arthritis hospitalized for interstitial lung disease. Chest, 1988; 93: 114–18
9. Symmons D, Barrett EM The incidence of Rheumatoid arthritis in the UK; Brit J Rheumatol 33, 735-739.
10. Albani S and Carson DA. Etiology and pathogenesis of Rheumatoid arthritis. In Koopman WJ. Arthritis and allied conditions. A textbook of rheumatology, 13th ed, pp 979-992 Baltimore: Williams and Wilkins.

11. Turesson C, Jacobsson L, Bergstrom U et al: Predictors of extra-articular manifestations in rheumatoid arthritis. Scand J Rheumatol, 2000; 29(6): 358–64
12. Van Zeben D,Hazes JMW. Association of HLA in Rheumatoid arthritis. Arthritis Rheum 34, 822 – 830.
13. Salvarani C, Macchioni P, Mantovani W et al: Extraarticular manifestations of rheumatoid arthritis and HLA antigens in northern Italy. I J Rheumatol, 1992; 19(2): 242–46
14. Boire G, Menard HA: Clinical significance of anti-Ro (SSA) antibody in rheumatoid arthritis. J Rheumatol, 1988; 15(3): 391–94
15. Kerstens PJ, Boerbooms AM, Jeurissen ME et al: Accelerated nodulosis during low-dose methotrexate therapy for rheumatoid arthritis. An analysis of ten cases. J Rheumatol, 1992; 19(6): 867–71
16. Friestein GS. Etiology and pathogenesis of rheumatoid arthritis. Textbook of rheumatology, 5th ed, pp 851- 897. Philadelphia : WB Saunders.
17. Jacobsson LTH, Hanson RL, Knowler WC et al: Decreasing incidence and prevalence of rheumatoid arthritis over a 25-year period. Arthritis Rheum, 1994; 37: 1158–65
18. Doran MF, Pond G, Crowson CS et al: Trends in the incidence and mortality in rheumatoid arthritis in Rochester, Minnesota, over a 40-year period. Arthritis Rheum, 2002; 46: 625–31
19. Heikillä S, Isomäki H: Long-term outcome of rheumatoid arthritis has improved. Scand J Rheumatol, 1994; 23: 13–15
20. Bergström U, Book C, Lindroth Y et al: Lower disease activity and disability in Swedish patients with rheumatoid arthritis in 1995 compared with 1978. Scand J Rheumatol, 1999; 28: 160–65
21. Emery P. Rheumatoid arthritis: not yet curable with early intensive theraphy: Lancet 350, 304-305.

22. Wanchu A, Suri L, Deodhar SD et al: Extra-articular manifestations among north Indian patients with rheumatoid arthritis. Journal of Indian Rheumatism Association, 1997; 5(3): 75–78
23. Agrawal V, Usha, Goel SC, Gupta RM: A probable explanation for mild extra-articular manifestations in Indian patients of rheumatoid arthritis: a preliminary study. Indian J Pathol Microbiol, 1998; 41(3): 297–301
24. Buth BA, Bisati SD: Clinical and immunogenetic profile of rheumatoid arthritis patients in Kashmir. JK Practitioner. 1995; 2(3): 111–13
25. Bijsma JWJ and Velthius PJ Rheumatoid arthritis: Multi- Systemic Auto Immune Diseases: An Integrated Approach, pp 141 -172. Amsterdam; Elsevier.
26. Arnett FC, Edworth SM et al: The American Rheumatism Association 1987 revised criteria for the classification of rheumatoid arthritis. Arthritis Rheum, 1988; 31: 315–24
27. Hochberg MC, Chang RW, Dwosh I et al: The American College of Rheumatology 1991 revised criteria for classification of global functional status in rheumatoid arthritis. Arthritis Rheum, 1992; 35: 498–502
28. Soltys AJ and Axford JS. Rheumatoid factors: where are we now? Ann Rheum Dis 56. 281 -286.
29. Felson DT, Anderson JJ, Boers M et al: The American College of Rheumatology preliminary core set of disease activity markers for rheumatoid arthritis clinical trials. Arhtritis Rheum, 1993; 36:
30. Cats A and Hazevoet HM. The Significance of positive tests for rheumatoid factor in prognosis of RA. Ann Rheum Dis 29, 254-260.
31. Melbye, Gonzalez-Alvaro I, Balsa A et al: Immuno pathology of subcutaneous rheumatoid nodules. Ann Rheum Dis, 2003; 62: 897–900

32. Hale and Haynes: pathology of Rheumatoid arthritis. In Koopman WJ. Arthritis and allied conditions. A textbook of rheumatology, 13th ed, pp 993-1016. Baltimore: Williams and Wilkins.
33. Scott DL: Interstitial Lung Disease and Disease Modifying Anti Rheumatic Drugs. Lancet, 2004; 363: 1239–40
34. PearsonJK, Graham DR, Desmond J et al: Rheumatoid nodules of Spine. Rheumatology (Oxford), 2002; 41: 262–67
35. Bodineau JL, Becerra ER, Dominguez AC et al: Serum neutrophil elastase levels predict initial clinical condition but do not correlate with the progression of interstitial lung disease. Med Sci Monit, 2003; 9(1): CR1–CR5
36. Carulli MT, Davies UM: Peripheral neuropathy: an unwanted effect of lefl unomide? Rheumatology, 2002; 41: 952–53
37. Chalk CH, Dyck PJ and Conn DL: Vasculitic neuropathy. Rheumatology (Oxford), 2004; 43: 934
38. Rajesh M, Sulochana KN, Sundaram AL et al: Presence of a 88 kDa Eales protein in uveitis, tuberculosis, leprosy and rheumatoid arthritis. Med Sci Monit, 2003; 9(2): CR95–CR99
39. Hart, F. D., Golding, J. R., and Mackenzie, D. H., Annals of the Rheumatic Diseases, 1957, 16, 471.
40. Pincus, and Golding, Prevalence of depression in Rheumatoid Arthritis. J Bone Joint Surg 63, 342-350.
41. Pallis, C. A., and Scott, J. T., British Medical Journal, 1965, 1, 1141.
42. Chamberlain, M. A., and Bruckner, F. E., Annals of the Rheumatic Diseases, 1970, 29, 609.
43. Gilliatt, R. W., Proceedings of the Royal Society of Medicine, 1966, 59, 989.

44. Weller, R. O., Bruckner, F. E., and Chamberlain, M. A., Journal of Neurology, Neurosurgery, and Psychiatry, 1970, 33, 592.
45. Cruickshank, B., Annals of the Rheumatic Diseases, 1954, 13, 136.
46. Scott, J. T., et al., Annals of the Rheumatic Diseases, 1961, 20, 224.
47. Herbison GJ, Ditunno JF, Jaweed MM. Muscle atrophy in rheumatoid arthritis. J Rheumatol 1987; 14 Suppl 15:78–81.
48. Johnson RL, Smyth CJ, Holt GW, Lubchenco A, Valentine E. Steroid therapy and vascular lesions in rheumatoid arthritis. Arthritis Rheum 1959; 2:224–49.
49. Bunim J. Peripheral neuropathy in rheumatoid arthritis. Bull Rheum Dis 1961; 9:251–4.
50. Ochoa J, Torebjorg HE. Sensations evoked by intraneural micro stimulation of single mechanoreceptor units innervating the human hand. J Physiol (Lond) 1983; 342:633–54.
51. Wees SJ, Sunwood IN, Oh SJ. Sural nerve biopsy in necrotizing vasculitis. Am J Med 1981; 71:525–32.
52. Castaldo JE, Ochoa J. Peripheral nerve: structure, function and dysfunction. In Kelley WN, Harris ED Jr, Ruddy S, Sledge CB, editors. Textbook of rheumatology. 2nd ed. Philadelphia: WB Saunders; 1985. p. 295–313.
53. Olney RK. AAEM minimonograph #38: neuropathies in connective tissue disease. Muscle Nerve 1992; 15:531–42.
54. Lanzillo B, Nucciotti R, Crisci C, Pappone N, Di Caprio G, Scioli M, et al. Carpal tunnel syndrome (CTS): a six month post surgical follow up [abstract]. International Congress of Electroencephalography and Clinical Neurophysiology; 1993 Aug 29–Sep 4; Vancouver, Canada. Electroencephalogr Clin Neurophysiol 1993; 2: S114.
55. Nucciotti R, Lanzillo B, Crisci C, Pappone N, Di Caprio G, Scioli M, et al. Congress of Italian Society of Neurophysiology; 1996 May 15–18; Ischia, Italy.

56. Rosenbaum RB, Ochoa JL. Carpal tunnel syndrome and other disorders of the median nerve. Boston: Butterworth-Heinemann; 1993.
57. Hart F D, Golding J R, MacKenzie D H. Neuropathy in rheumatoid disease. Ann Rheum Dis 1957; 16: 471-80.
58. Gordon DA, Stein DL. The extra-articular features of rheumatoid arthritis. Am J Med 1973; 54: 445-52.
59. Nakano K K. The entrapment neuropathies of rheumatoid arthritis. Orthop Clin North Am 1975; 6: 837-60.
60. 60Giovanni AL, Albani TA, The clinical and electrophysiological evaluation of Rheumatoid arthritis. J Pheri Nerv Sys 2006; 32: 45-46
61. Barnes C G, Currey H L F. Carpal tunnel syndrome in rheumatoid arthritis. A clinical and electro diagnostic study. Ann Rheum Dis 1967; 26: 226-33.
62. Uoyd K, Agrawal A. Tarsal-tunnel syndrome, a presenting feature of rheumatoid arthritis. Br Med J 1970; iii: 32.
63. Chater E H. Tarsal-tunnel syndrome in rheumatoid arthritis. Br Med J 1970; iii: 406.
64. Conn DL, Dyck PJ: Angiopathic neuropathy in connective tissue disease. Dyck PJ, Thomas PK, Lambert EH, Bunge R (Eds.): Peripheral neuropathy: Philadelphia, WB Saunders; 1984: 2027-43.
65. Sivri A, Guler-Uysal F: The electroneurophysiological findings in rheumatoid arthritis patients. Electromyogr Clin Neurophysiol 1999; 39 (7): 387-91.
66. Toussirot E, Serratrice G, Valentin P: Autonomic nervous system involvement in rheumatoid arthritis. 50 cases. J Rheumatol 1993; 20 (1508-14).
67. Shinoda J, Hashizume H, McCown C et al.: Carpal tunnel syndrome grading system in rheumatoid arthritis. J Orthop Sci 2002; 7(2): 188-93.

68. Unal O, Ozcakar L, Cetin A, Kaymak B. Severe bilateral carpal tunnel syndrome in juvenile chronic arthritis. Pediatr Neurol. 2003 Oct; 29(4): 345-8.
69. Sivri A, Guler-Uysal F: The electroneurophysiological evaluation of rheumatoid arthritis patients. Clin Rheumatol 1998; 17(5): 416-8.
70. Lang AH, Kalliomaki JL, Puusa A, Halonen JP. Sensory neuropathy in rheumatoid arthritis: an electroneurographic study. Scand J Rheumatol. 1981; 10(2): 81-4.
71. Pinal RS, Masi AT, Larsen RA: Preliminary criteria for clinical remission in rheumatoid arthritis. Arthritis Rheum 1981; 24 (10): 1308-15.
72. Steinberg VL. Neuropathy in Rheumatoid disease. Brit Med J 1960; 2: 1600-3
73. Jablecki CK, Andary MT, So YT, Wilkins DE, Williams FH: Literature review of the usefulness of nerve conduction studies and electromyography for the evaluation of patients with carpal tunnel syndrome. AAEM Quality Assurance Committee. Muscle Nerve 1993; 16(12): 1392-414.
74. DeLisa JA, Lee HJ, Baran EM, Lai KL, Spielholz, N: Manuel of nerve condition velocity and clinical neurophysiology. 3rd ed., New York, Raven Pres, 1994: 70-81.
75. Marshall SC and Murray WR. Deep radial nerve palsy associated with rheumatoid arthritis. Clin Ortho Relat Res 103, 157-162.
76. Werner RA, Andary M: Carpal tunnel syndrome: pathophysiology and clinical neurophysiology. Clin Neurophysiol 2002; 113 (9): 1373-81.
77. Padua L, Lo Monaco M, Padua R, Gregori B, Tonali P: Neurophysiological classification of carpal tunnel syndrome: assessment of 600 symptomatic hands. Ital J Neurol Sci 1997; 18 (3): 145-50.

78. Lanzillo B, Pappone N, Crisci C, di Girolamo C, Massini R, Caruso G. Subclinical peripheral nerve involvement in patients with rheumatoid arthritis. Arthritis Rheum. 1998 Jul; 41(7): 1196-202.
79. Scott DG, Bacon PA, Tribe CR: Systemic rheumatoid vasculitis: a clinical and laboratory study of 50 cases. Medicine 1981; 60 (4): 288-97.
80. El M, Ashour S, Moustafa H, Ahmed I: Altered levels of soluble adhesion molecules in patients with rheumatoid arthritis complicated by peripheral neuropathy. J Rheumatol 2002; 29 (1): 57-61.
81. Kissel JT, Riethman JL, Omerza J, Rammohan KW, Mendell JR: Peripheral nerve vasculitis: immune characterization of the vascular lesions. Ann Neurol 1989; 25(3): 291-7.
82. Bekkelund SI, Mellgren SI, Proven A, Husby G: Quantified neurological examination with emphasis on motor and sensory functions in patients with rheumatoid arthritis and controls. Br J Rheumatol 1996; 35(11): 1116-21.
83. Dumitru D: Focal Peripheral Neuropathies. In Electrodiagnostic Medicine. Dumitru D(Eds.): Philadelphia, Hanley & Belfus 1995: 851-927.
84. Nadkar MY, Agarwal R, Samant RS, et al.: Neuropathy in rheumatoid arthritis. J Assoc Physicians India 2001; 49: 217-20.
85. Chang DJ, Paget SA. Neurologic complications of Rheumatoid arthritis. Rheum Dis Clin North Am 1993; 19; 955-73.
86. Kar M, Mukherjee S, Mandal D. Neuropathy in Rheumatoid Arthritis: Clinical and electrophysiological observations. Bull Indian Rheumatism Assoc 1991; 5; 80-2.
87. McCombe PA, Klestov AC, Tannenberg AE. Sensorimotor Peripheral Neuropathy in Rheumatoid Arthritis. Clin Exp Neurol 1991; 28: 146-53.

88. Vollertsen RS, Conn DL, Ballard DJ. Rheumatoid vasculitis: survival and associated risk factors. Medicine 1986; 65: 365-75.

PROFORMA

THE CLINICAL AND ELECTROPHYSIOLOGICAL EVALUATION OF PERIPHERAL NEUROPATHY IN RHEUMATOID ARTHRITIS

NAME:

AGE:

SEX:

MIN NO.:

RCC NO.:

DURATION OF RA:

DURATION OF SYMPTOMS OF NEUROPATHY:

FUNCTIONAL GRADE OF RA:

RADIOLOGICAL GRADE OF RA:

NEUROPATHY SYMPTOMS:

NEUROPATHY SIGNS

NSS SCORE:

NDS SCORE:

EXTRA-ARTICULAR MANIFESTATIONS:

R.F.:

ESR:

CRP:

H/O DM:

H/O ALCOHOLISM:

FBS/PPBS:

HIV:

UREA/CREATININE:

NCS:

THERAPY: